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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Administrative Patent Judge Sally Gardner Lane

JEAN-LOUIS RUELLE
Junior Party
(Patent 6,780,419
Application No. 10/896,778),

v.

VINCENZO SCARLATO, VEGA MASIGNANI, RINO RAPPUOLI,
MARIAGRAZIA PIZZA, and GUIDO GRANDI
Senior Party
(U.S. Application 11/212,443).

Patent Interference No. 105,551

Oral Hearing Held: April 15, 2010

Before SALLY G. LANE, RICHARD E. SCHAFER and MICHAEL P. TIERNEY, *Administrative Patent Judges.*

APPEARANCES:

ON BEHALF OF RUELLE:

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PROCEEDINGS

JUDGE LANE: We're here for oral argument in interference 105,551, Ruelle v. Scarlato, and we'll start with Junior Party. Mr. Olstein, can you tell us who you have with you?

MR. OLSTEIN: Yes. Elliot Olstein representing the Junior Party. Mr. Lillie of my firm is also present as counsel. And from the Client, GSK, Alice Bradney and Michael Leanski (ph.).

JUDGE LANE: All right. Mr. Kreeger?

MR. KREEGER: Good afternoon, Your Honor. Matthew Kreeger from Morrison & Foerster. With me from my firm is Otis Littlefield.

JUDGE LANE: Thank you. Okay. I think in the order it said each side would have 20 minutes, right? So we'll start with Junior Party, and, Mr. Olstein you can reserve appropriate time for rebuttal, if you'd like.

MR. OLSTEIN: Your Honor, I will be proceeding one motion at a time, as we did in the previous proceedings; that first we would argue the Ruelle priority motions, then after that, follow that by arguing --

JUDGE LANE: Well, you would reserve time for your rebuttal if you want to rebut, I suppose, the Scarlato priority case. So you're going to argue your priority case at this time.

MR. OLSTEIN: Just my priority case?

JUDGE LANE: Yes.

MR. OLSTEIN: Thank you, Your Honors. For the --

JUDGE LANE: I'm sorry --

MR. OLSTEIN: Okay. I just wanted to be sure we're set.

JUDGE LANE: Okay. I'm sorry.

MR. OLSTEIN: No, it's fine. For the Ruelle priority case --

JUDGE LANE: Do you want to save some time? How do you want to split up your time?

MR. OLSTEIN: Well, I would like to save time, but may I just have a little clarification? I'm going to present my priority case first. Mr. Kreeger is going to then answer my priority case, and then present his priority case?

JUDGE LANE: Right. And then any -- yes, and then he can reserve a little time for something that he may have in reply.

MR. OLSTEIN: Then I can rebut?

JUDGE LANE: Well, no, we're not going to go on and on, but --

JUDGE SCHAFER: Two and two?

JUDGE LANE: Yeah, two and two. Thank you.

JUDGE SCHAFER: You get a chance to present your case.

MR. OLSTEIN: Yes.

JUDGE SCHAFER: Then they'll present theirs. Then you'll get a chance to rebut, and then he'll get a chance to rebut. So it's just -- both of you will get -- since you both have motions, you'll each get an opportunity to present your case and a rebuttal.

JUDGE LANE: Is your confusion that you don't know whether you should speak about your opposition in the first part of your argument?

MR. OLSTEIN: Well, yes, because the last time when we proceeded, we took one motion at a time.

JUDGE LANE: Oh, when we were doing nonpriority motions?

MR. OLSTEIN: Yeah. And what we did is the Junior Party presented his motions in toto, then there was a reply, and then there was a rebuttal, and then the Senior Party -- and that's -- I'll do it any way Your

Honors would like us to do it. I'm just trying to find out what is the procedure so I know how to reserve.

JUDGE LANE: Okay. Well, let's do it this way: Let's hear your priority case, and then we'll give you some time in rebuttal. I just wanted to kind of see how much time you wanted for each portion of your argument.

MR. OLSTEIN: Okay. Well, --

JUDGE LANE: What do you think?

MR. OLSTEIN: If I get 20 minutes, I will take -- approximately split it in half.

JUDGE LANE: All right.

MR. OLSTEIN: Maybe reserve a little --

JUDGE LANE: We may have a lot of questions, anyway.

MR. OLSTEIN: Yeah.

JUDGE LANE: Continue.

MR. OLSTEIN: So in any event, in the Ruelle priority case, there are really only two issues that are before this Board. Conception has been conceded, so the issues that are left is whether or not -- and our February reduction to practice has also been conceded. So the two issues in this is what I call our first or initial reduction to practice and diligence. For our initial reduction to practice, we rely on work that was performed prior to the constructive filing date of the Scarlato priority case, but because of the statements that were put in, even if we prove that case, we will only get a date after his priority filing, which would be -- his priority filing was January 14th, and we would get January 16th.

So with respect to the first reduction of practice, Dr. Pullen, who performed the work on behalf of Inventor Ruelle, testified that he

understood and believed he had produced a polypeptide within the count in December 1997.

JUDGE SCHAFER: Tell me what that means, within the count, because I look at the count, you have a full -- there's a full amino acid sequence, and then there's this 15 contiguous amino acids. Which --

MR. OLSTEIN: Well, he produced a fragment of the entire sequence.

JUDGE SCHAFER: So you're focusing on one of the -- that you had 15 --

MR. OLSTEIN: Part B of the count.

JUDGE SCHAFER: Yeah, 15 contiguous amino acids.

MR. OLSTEIN: Correct, Your Honor.

JUDGE SCHAFER: Of the particular sequence.

MR. OLSTEIN: Yes.

JUDGE SCHAFER: Okay.

JUDGE LANE: Mr. Olstein, when I was first reading your Bief, it seemed to me like you were saying that they had taken this vector and put it into the E. coli cells, and then they kept them at a certain temperature so as not to express the protein. So now you're -- in this December work. So is that what happened? I mean, how did they -- it seemed more, maybe, in your Reply you talked about this leaky thing. So I was trying to figure out where you talk about, in your Initial Brief, where they actually express the protein.

MR. OLSTEIN: Well, it's in the Initial Brief and it's in Dr. Pullen's Declaration, initially. His paragraphs 48, 55 to 60, 70 and 80 explain that he did understand that he had expressed polypeptide as of that December '97 date. And because of the fact that there was an inhibitor in there, normally,

these inhibitors are supposed to express only when you elevate temperature. But Dr. Pullen had a lot of experience with this particular type of expression system, and based on that experience, he knew that even though you only maintained it at 30 degrees C, so-called leakiness. In other words, there would be expression. So he prepared a vector for the express purpose of expressing the polypeptide of the count. He had --

JUDGE LANE: So let me get back to that. So it's like an incidental expression? Because it seemed to me like he didn't intend to express it, he intended to not express it by keeping it at the certain temperature.

MR. OLSTEIN: Well, he inherited a vector system, okay, that he had experience with. That vector system did have the inhibitor, and the intent of whoever initially developed that vector system would have been so as to express only at 39 degrees C. But what he testified was that he had previously used that same type of expression system that had that same type of inhibitor, and he knew that even if he was at 30 degrees C, he would be getting expression because of his prior experience with that particular system.

JUDGE LANE: Did he actually do some sort of a test to confirm that he did get protein?

MR. OLSTEIN: He did not do a test at that time to confirm that the protein -- but based on the fact that this was a well-known expression system and that he had used it numerous times in the past, he knew that at 30 degrees C, he would get expression from that system. And what he had done was test the actual vector to make sure that he had the DNA in the vector. He had tested the E. coli cells to make sure that the vector was in the E. coli cells. And based on his prior experience knowing how the biological

systems work and they normally express protein once you have it in the correct orientation, and once you know that it is in the E. coli, and once he knew that this type of expression system would express at 30 degrees C, his testimony was that he knew and understood at the time that he had expressed polypeptide --

JUDGE SCHAFER: Well, what you're saying is he has a belief that it was there. Can you cite a case that says, for an actual reduction to practice, the person doing the test, his belief that he got some is sufficient as opposed to actual proof that he actually got the stuff?

MR. OLSTEIN: Well, what we have done is produce evidence to show that it did in fact express at that time, although that was subsequent evidence to confirm. This is confirming evidence that it actually did work, because that set of cells --

JUDGE SCHAFER: So you did -- so you subsequently did the same thing? You took the same vector, the same critter with the vector and -- at 30 degrees and then tested what you got, and you ended up showing that the protein was there?

MR. OLSTEIN: Yeah. Not to mislead, Your Honor; that confirmatory test was not a contemporaneous test.

JUDGE SCHAFER: Right. I understand.

MR. OLSTEIN: It was done in 2009.

JUDGE SCHAFER: Yeah, there's plenty of case law that says you can test something later to show that you had some property of a compound or something. But that's what your case is, actually, is that here's what we did at the time, the person who did the test believed they had it, and then

subsequent tests under that condition show that his belief was in fact correct?

MR. OLSTEIN: That is correct, Your Honor.

JUDGE SCHAFER: Okay.

MR. OLSTEIN: And what we have done was place into evidence, confirmatory as we call it, that 2009 test, and we also placed into evidence his experience and his knowledge that this was leaking, as Judge Lane called it, and as we call it, in fact did produce -- there was literature contemporaneous. Not that he knew of it at the time, but just as confirmatory evidence to indicate that it was already known in the art that this type of promoter system did leak, even when at 30 degrees C. So it's confirmatory evidence to support the credibility of his testimony as opposed to providing evidence that he knew and believed it. And, Your Honors, I want to point out that at no time in this case, although Scarlato had ample opportunity, did they provide any evidence, any expert testimony, any cross-examination testimony that challenged the tests that were done in 2009, challenged or indicated that this promoter was not a leaky system, no evidence to that effect, challenged -- they had opportunity to cross-examine Dr. Puller that in fact he had this belief and this understanding. They didn't challenge or provide any evidence that he hadn't had this prior experience. So it all stands unrebutted, all of this evidence. So what have they challenged?

I'm watching my timing. Excuse me.

They cite nunc pro tunc cases which are not apposite to this situation. Because in the nunc pro tunc cases that they cited, there was no evidence that there was an appreciation at the time that there was this expression. In

all of those cases, somebody had to go back and then demonstrate that he could have appreciated, or the Inventor could have had this appreciation at the time because it was there. But his unrebutted testimony that he did know it, he did understand it, he did believe it, and he provided -- we have provided ample evidence to show that it was credible because it was known.

I don't know how much of my time I've used of the 10.

JUDGE LANE: Go ahead. We had a lot of questions there. I'll let you go on.

MR. OLSTEIN: Okay. So now on the diligence question, all right?

JUDGE SCHAFER: So let me go back to what the count says. So what he believed at the time, and what you showed later, that you proved later was that what was expressed was 15 contiguous amino acids of your sequence, at least 15 contiguous?

MR. OLSTEIN: Well, it was a lot more.

JUDGE LANE: Right, right.

MR. OLSTEIN: When you look at the sequence comparison --

JUDGE SCHAFER: I'm familiar how people right claims.

MR. OLSTEIN: Yeah. It was a very long sequence that we actually demonstrated.

JUDGE SCHAFER: Okay. And then, also, what about the basis for, when it's administered to a subject, that it would -- induces an antibody or T cell mediate immune response? That's part of the Count Two, particularly that Part B.

MR. OLSTEIN: Well, in this case, neither side did any testing at the time, but neither side had challenged that once you knew you had this polypeptide, that it would induce an antibody response.

JUDGE SCHAFER: Is the idea that if you put anything that's truly foreign into a body, it's going to --

MR. OLSTEIN: Essentially, that's --

JUDGE SCHAFER: Yeah, okay. I see your position.

MR. OLSTEIN: Yeah. And by the way, we haven't challenged Scarlato's position on that, and they didn't do any testing, either, to show that an antibody was produced. If I may just get a couple of minutes to address the diligence part of our primary case, it goes as follows: Dr. Ruelle did not have a laboratory. He's the Inventor. He came up with the sequence. And so he had to rely on the central laboratory, which Dr. Pullen was the head, was the chief. Dr. Pullen didn't normally do laboratory work, but the testimony that came in, again unchallenged, is that due to prior projects that were present, there was nobody available to do the work. So what did Dr. Pullen do? He volunteered, even though he doesn't normally do bench work, to not delay this project, to start doing some laboratory work. But he also testified, as head of the laboratory, he couldn't devote full time to doing this work because of the fact that he had to attend to his normal duties. And he outlines all these normal duties: lab reports, meetings, outside meetings, et cetera, et cetera, et cetera.

So what happens here is he did not work full time on doing the work for Ruelle, the Inventor. We cited two cases that indicate that when you have someone that's not the Inventor doing the work because you have to rely on somebody else, and that you only have to exercise reasonable diligence, that there is some slack. So for example, in the Ray-Bellet (ph.) case that we cited in our Brief, in which they had to send the compounds for testing in another laboratory, there was a long delay in being able to do the

work. In the Des Solms v. Schoenwald (ph.) case, 15 U.S.P.Q. 2nd, 1507 -- and the Ray-Bellet case, by the way, is 493 F.2d. 1380 -- a graduate student was working, the graduate student could only work part time, and that was considered good enough.

So, if you look at the overall work that was done, yes, there are times and periods when Dr. Pullen was working on his normal duties. He effectively was a party-time voluntary person performing lab work. And reasonable diligence doesn't require that he ignore his normal duties because he took on, voluntarily, to do work on this project. And therefore, it's basically our position, and outlined in more details, obviously, in our papers, that there was reasonable diligence considering that Dr. Pullen was part-time working on the project only because he had all these other duties.

The only other thing I wanted to add on the diligence aspect, Scarlato argued that Dr. Pullen, when he said he was attending to these other duties, couldn't associate a specific day with a specific duty. That's true, but remember how long ago this was. What Dr. Pullen did testify to, and none of it, again, challenged, is here are my normal work duties, and gave five or six different categories. He then said that I know on those days I was doing one of those duties, but I can't tell you specifically that it was a lab meeting, or an outside meeting, or providing reports that I had to do, or supervising, or helping a laboratory person working on a project, assist them in another project; I couldn't necessarily identify that specifically. But he did identify the type of work and the days on which he did it. And if you go through the diligence chart, you will see all throughout the project, when he started in November, for which we don't have to show diligence, there are always

periods of time that he was not working on this specific project and attending to other duties.

So, the overall pattern is consistent; that basically, because he was head of the laboratory, he could not devote full time to working on the project, and because the other people in his laboratory had already been working on previous projects. So instead of sitting it and putting it aside and waiting until those previous projects were finished, he took up the work, he did it, but he could only do it on a part-time basis because of his other duties.

JUDGE SCHAFER: I don't remember from his testimony, did he testify that he worked on it at every opportunity that he had, that he could work on it?

MR. OLSTEIN: Basically, yes. I cannot give you an exact quote, but what he basically said, he had to attend to these other duties, he had all of these other duties, and that there was no one else in the laboratory who could do it at the time. And if you look at the pattern, you will see that there are certain times of the month when there's 4 or 5 or 6 or 7 days, whatever it was -- working days I'm talking about -- when he wasn't working on the project but he carefully described all the other duties that he had at the time, and that he was working as best he can.

Where does it say that?

MR. LILLIE: Right in the last sentence of paragraph 7 of --

MR. OLSTEIN: Mr. Lillie pointed out to me, because I didn't remember it by heart, on page 4 of his Declaration, he said, "If I had not been involved in these matters during such period, I would have been able to perform laboratory work on Dr. Ruelle's project, and I would have done so." So I think that answers Your Honor's question.

JUDGE TIERNEY: Before we go, I do have a question about the confirmatory testing.

MR. OLSTEIN: Yes.

JUDGE TIERNEY: And I take it that it's your belief that it was not required in order to get the -- reduction of practice -- in December?

MR. OLSTEIN: That it was not --

JUDGE TIERNEY: I'm looking at the argument here, and that was -- they didn't do the confirmatory test of the expression until a later date.

MR. OLSTEIN: That's correct.

JUDGE TIERNEY: So at this point, we are -- your actual reduction of practice is based on speculation, however reasonable, that this would actually express in the fashion you say it did?

MR. OLSTEIN: I would not call it speculation.

JUDGE TIERNEY: But are we certain --

MR. OLSTEIN: I would say based on experience --

JUDGE TIERNEY: But are we certain to 100 percent that this actually did occur, or are we basically just saying it's reasonable to assume?

MR. OLSTEIN: Well, I would say that at the time he was certain to 100 percent that the whole group of cells -- now, since you raised the question, if you give me one minute, I'll explain that part of it to you. There is evidence in the record, all right, about clones that didn't work, all right? And Mr. Kreeger, in Scarlato, did cite that work, and that's true. But you have to understand what it means. What we were relying on is a collection of cells. You take a collection of E. coli cells, you transform them with the vector. It may occur that some of the cells do not work and express. And when you isolate a clone, what you're doing is taking a single cell and

growing it up and then testing it. So the fact that 1 cell, 2 cells, 5 cells in this whole collection doesn't express doesn't raise an inference that the collection of cells do not express. And from his prior experience in working with it -- and again, at this point, biotech wasn't magic. It was kind of known that if you isolate the DNA, you put it in the vector in the right order so that it's in line with the promoter, you will get that expression.

JUDGE TIERNEY: I understand you're saying there's a reasonable belief that expression occurred. But to what extent is it a reasonable belief versus a certainty? Can you address that?

MR. OLSTEIN: I don't know if anything is certain in life, but as close as you can be. In other words, the unusual could always happen. At that point, what they're talking about is an unusual occurrence; that if you got zero expression. Is there always a possibility? Yes. But the confirmatory tests show that didn't occur. And I may also point out that a couple of months afterwards, when they did it at the 39 degrees C and took the same vector system, they demonstrated it expressed. It wasn't at the 30 degrees C, but it did confirm soon thereafter that the --

JUDGE LANE: So when they did the testing in February, they still never did the testing where they were searching for expression at 30 degrees?

MR. OLSTEIN: That is correct. It was at 39 degrees.

JUDGE LANE: So that's what you're relying on for your actual reduction, the practice is expression at 30 degrees?

MR. OLSTEIN: That is correct. But what the 39 degree test shows is that the vector was put together right, there wasn't an inherent defect in the vector, that it wasn't something that made it incapable of expressing, that it,

you know, it was just a rotten vector or something like that. And it's the confirmatory test -- again, we're not relying on that for his understanding, contemporaneous understanding at the time, it's just to show that his contemporaneous understanding was correct and that his testimony is credible.

JUDGE LANE: I understand.

MR. OLSTEIN: Thank you.

JUDGE LANE: Thank you. Mr. Kreeger?

MR. KREEGER: Thank you, Your Honor. These are just exhibits that are already in the record, but I was going to refer to. May I approach?

JUDGE LANE: Sure. Mr. Olstein has a copy?

MR. KREEGER: He does.

JUDGE LANE: Do you have a copy?

MR. OLSTEIN: I do. Thank you.

MR. KREEGER: I'd like to begin with the Ruelle motion, and I'd just like to point out, for starters, that, although this may be apparent, if the Board agrees with Scarlato on either of our motions, either the Ruelle motion or the Scarlato motion, then Scarlato is entitled to prevail in this case.

First, with respect to the Ruelle motion, on the reduction to practice that you've been discussing, the supposed December 1997 experiments, the count in this case is directed to a polypeptide. And there is not data, as Mr. Olstein acknowledged, no data in their notebooks that shows that a polypeptide was expressed in December 1997. So instead, their argument is we constructed the DNA which codes for that polypeptide, inserted it into these E. coli cells, with an experiment design that was set up so that those

cells would not express at 30 degrees. That was the point of this suppressor. They were left at 30 degrees until February, at which point they raised it, expressed it, and tested it. So if you look at the entire experimental record, what you see is a set of experiments with a clear experimental design to prevent expression until February, then in February to express. There was never any testing done in the relevant time period of the cells that were maintained at 30 degrees until the interference began in 2009, when they did some experiments.

So I think we're in the classic situation here where there's been an attempt to reconstruct a reduction to practice after the fact. We do have Dr. Pullen's bare testimony that he personally believed there was expression at 30 degrees, but there is no contemporaneous document that backs that up, and the experimental design is fundamentally inconsistent with that. If he had that belief, then he should have taken those, and he would have taken, those cells at 30 degrees and had them tested. He simply did not do that.

And what's more, to the extent he had that belief, it simply wasn't reasonable. And I'd like to just point out --

JUDGE LANE: Mr. Kreeger, let me just -- before you do that, let me see, because I want to make sure I have this straight. Was it at some point, maybe it was in April, the testing was done at 30 degrees to see if some expression would occur?

MR. KREEGER: In April 2009.

JUDGE LANE: Okay.

MR. KREEGER: After the interference began.

JUDGE LANE: Okay.

MR. KREEGER: Then, at the direction of counsel, there were some experiments performed.

JUDGE LANE: And that did result in expression?

MR. KREEGER: Using some very sensitive detection techniques which they didn't have, or weren't even available, and certainly didn't employ, back in 1997, they were able to PCR out, or use very sensitive measures to find some very low levels of expression in 2009. But there is no evidence that that was known at the time.

And that's the point I wanted to make, too, Your Honor, is if you look at -- you'll see in Exhibit 20038 we've taken excerpts from Dr. Pullen's own notebook. So there's the cover page. The next page is from the February 1998 experiments done with the 39 degrees samples. And actually, there's three different antigens being investigated here. You'll see Orph 1-5 (ph.), Orph 7, and HSF-like (ph.) fragment. The HSF-like fragment is the one that's at issue in this interference. But at the same time that they were testing that antigen, they were also testing vectors that were constructed to express different antigens. And what he did in each case is he made six clones for each of these three antigens and he tested all 18 clones, and all of them had been selected so that they supposedly had the right insert. There was selection process so each one of them had the right insert and was expected to express. And if you look at the results he got, with Orph 1-5, there was no expression, zero for six, and this was after the cells had been raised to 39 degrees. For Orph 7, he got one out of six correct. And then if you look at page 51, the next page, that's the HSF-like fragment, which shows that, sure enough, in one out of the six clones, he got expression of the HSF-like fragment at issue in this interference.

And we don't contest that they actually got it in February. I mean, we acknowledge that this experiment shown on page 51 demonstrates that they made the protein of the count in February. But what you see here is an experimental design that even when they performed it at 39 degrees as designed, they often did not get expression. In the case of the Orph 1-5, they got no expression. So his subjective belief that, oh, yes, this is leaky and I'm bound to get expression is just simply not true. Even in the experiments done at 39 degrees, they didn't always get expression. Because you can't know until you do the experiment. There was no question about that. All of the experts testified consistently, including the expert for Dr. Ruelle, that until you've done the experiment, you can't know whether you've expressed. So this subjective belief that, oh, yes, I'm sure I've got it, in addition to, frankly, being incredible, is not backed up by the data.

I'd like to move on to diligence unless there are further questions about the reduction to practice.

So if you look at the diligence chart which Ruelle has submitted, and I've attached it here, that's Exhibit 2064, the relevant time period here is -- the critical period starts on January 13th, 1998, just before Scarlato's constructive reduction to practice, and extends up to February 13th, 1998, the date of the reduction to practice. So if you look at the second page of Exhibit 2064, that has the relevant dates, and you'll see that between January 13th, '98 and February 13th, '98, that's 31 days of which there are six days that have an actual entry that indicates work on the invention. For the rest of the days, you've got Pullen attended to other work duties, Pullen does laboratory work on another project.

Now, the law is clear that the entire period had to be accounted for, either with activity or with a legally acceptable excuse. So we clearly do not have the entire period covered with activity, and there's including a two-and-a-half-week period between January 17th and February 4th, which Ruelle, in their brief, acknowledges there was no work done on the invention at all. So we clearly have gaps that have to be explained. And what is the explanation that's been given? All we have is the statements here in this report and in the testimony from Dr. Pullen that he attended to other work duties or worked on other projects. That is the extent of the specificity. And in the Bai vs. Laiko (ph.) case which we cited to, Your Honors, from this Board, it was clear that this kind of either activity or explanations have to be provided with specifics. It can't simply be a vague, oh, I was doing other work. And although he's described these various categories of work, there really is not much more specific than that. He had general duties and he chose to do those instead of this invention. That's just not enough.

Now, Rulle's argument is, well, Dr. Pullen isn't the Inventor, so they're excused, essentially, from showing diligence because Dr. Ruelle handed it off to Dr. Pullen, and then Dr. Pullen, whether he worked on it or not, was sort of out of Ruelle's hands. That's not the legal standard. This isn't the case where an Inventor sent a sample off for testing to some third-party laboratory and was at their mercy. In this case, GSK, the real party interest, employed both Dr. Pullen and Dr. Ruelle. And this is a case like in Bai vs. Laiko, where a single employer has to set priorities. And they clearly set priorities which made this a lower priority project. The testimony from Dr. Pullen was that although he was head of the lab, he had multiple scientists

and technicians working for him, and he had the option of assigning this project to any of them. He chose not to do that.

JUDGE LANE: Well, would it be necessary for diligence for them to drop everything else they're working on and just attend to this?

MR. KREEGER: What's required for diligence is that they attend to this project diligently, which means they can't decide as a matter of priorities to attend to a different project rather than this one. That's what the cases say: If they chose to do another invention rather than this one, that's the opposite of diligence. And that was definitely the case here.

And I'd just like to point out to one document that kind of confirms that. If you look at Exhibit 2067, this is a contemporaneous memo from December of 1997 that was submitted by Party Ruelle. And you'll see here that, on the very first page, there was a meeting of this group and the mission was to define and implement strategy to identify antigens for otitis media and meningitidis, which is, they were looking for antigens for this particular project. And then -- these pages aren't numbered, so it's going to be a little tricky to show you which page I want to talk about. I want to skip ahead to Addendum 1, which is about five or six pages in. Addendum 1 is a memo to J. Poolman from J. Pullen, Dr. Pullen, their corroborator, which is a summary of the projects that his team is working on. And you'll see that when it comes to neisseria meningitidis, he's got a list of different antigens they're interested in. There's 1.1, 2, 3, 4, 5, 6, 7, 8, 8 different antigens. Each of them is from a different part of the genome, and each of them is a separate project. And then the next page has a list of a Group B neisseria meningitidis vaccine candidates. Do you see that? I want to make sure we're all on the same page.

And you'll see there are five listed on the top, Orph 1-2, Orph 3-4, HPUA, LPDB, PILC, those five, then there's a line, then there's three more, Orph 5, Orph 7 and HSF. And again, HSF is the one at interest here. And then if you follow on, there's a detailed description of the first five candidates and what their plans are for them. There's several pages of the first five candidates. And finally, we get to this page which is a landscape page that says "Secondary NMB Vaccine Candidates," that's neisseria meningitis B, and you'll see that HSF is one of the secondary candidates. So if we look at the contemporaneous documents, we see that just as Dr. Pullen testified, they treated this antigen candidate as a promising one, but a secondary one. And that's the way he defined his priorities. Those were the priorities given to him by his employer, and that's the way he set his priorities when it came time to assign work in his laboratory. And this was definitely a low priority project, and the work that was done confirms that.

JUDGE SCHAFER: Well, is it your view that it has to be -- to be diligent, it has to be the highest priority?

MR. KREEGER: It has to be that -- there has to be either a legally sufficient explanation specifically about what was done instead of this project. And given the fact that there's no specifics, so it's very difficult to evaluate this as opposed to others, and given the evidence that this was not a high priority project, we suggest that's inconsistent with diligence.

All right, I'm going to turn to the Scarlato motion unless there's questions.

So this is an alternative way for Scarlato to prevail in the case. There actually was a prior conception that comes before the earliest date alleged by Ruelle, and if the Board agrees, then that is a completely alternative way for

us to prevail. Because having been the first to reduce as defined by the priority statements and the first to conceive, then Scarlato would prevail, with no showing of diligence being required.

So in this case, we have a conception. It was dated August 13th, 1997, and we submit that it was definite and firm and permanent because it included the specific sequence at issue. And actually, I might as well turn to that exhibit now. That's Exhibit 1106, the first one in our binder of exhibits. This is a sequence alignment dated August 13th, 1997 that includes a sequence from the meningitidis genome which has been aligned or compared with the HSF protein from an influenza bacteria. And based on this alignment, the Scarlato Inventors realized that they had a protein that was highly likely to be immunogenic because it was highly similar to an immunogenic surface protein expressed in a related influenza bacterium.

JUDGE LANE: Mr. Kreeger, before you were talking about this exhibit, how do we know -- or what do we take from that August 13th date? Is that the date this was printed out, is it the date the test was run, and how do we know what that means?

MR. KREEGER: Well, it's the date that the analysis was conducted that generated this document. The document was generated on August 13th, 1997. That's the testimony of Dr. Pot (ph.). I can't say that the printout was done that day, but the document itself was generated then.

JUDGE LANE: And Dr. Pot, he couldn't say as to this particular document?

MR. KREEGER: No, but based on the distinctive format of this document and his familiarity with the way these documents were generated, Chiron (ph.), he can say that this document was generated on August 13th,

1997 because that's the way the computer systems at Chiron at that time worked. Now, it might have been generated in a file that was since saved on a disk or a hard drive.

JUDGE LANE: There was a printout, but --

MR. KREEGER: I can't say there was a printout, but eventually it was printed out. The document was generated and the analysis was conducted on August 13th, 1997, based on the distinctive format of the document. I was going to deal with corroboration later, but I will come back to that.

JUDGE LANE: Okay. That's fine.

MR. KREEGER: But I wanted to first address a point made by Ruelle which we think can be easily dismissed. The claim is that this document, although it includes a specific polypeptide sequence, is not an actual definite and firm conception because the Inventor supposedly could not reasonably have been certain that their sequence was accurate. That's essentially the argument that Ruelle's making, and I think it's just fundamentally misdirected. This is not a question of reduction to practice, this is a question of conception. Did they have a definite and firm idea of a polypeptide within the scope of the count, and --

JUDGE LANE: Does the count require that this polypeptide be from the meningitis bacteria?

MR. KREEGER: No, what it requires is that -- you've seen the count. There's an alternative. In Alternative B, it requires that the sequence be at least 15 amino acids from the larger sequence and capable of inducing an immune reaction to the larger sequence. Now, it turns out, of course, they were looking for vaccine candidates that were from the meningitis bacteria,

and that was certainly their hypothesis, was that this sequence was from meningitis.

JUDGE LANE: But so long as you had a sequence that would produce a protein that would induce an immune response, you meet the count?

MR. KREEGER: Against the larger. Against the larger. And the testimony is that because of the length of the sequence, it would inherently, necessarily, induce an immune response that would recognize a larger protein of which it was a part. There is no question about that. But as for whether it was part of meningitis, for conception, all they needed was a hypothesis, and that clearly was their hypothesis. Whether they're right or not -- which, by the way, they were -- is part of reduction to practice. I mean, that's where the cases are quite clear.

In the cases that -- for example, Burrows Wilcom (ph.), which has a discussion about what it means for the conception to be definite and permanent, make it clear that what's required is that it be specific. The legal standard is that an idea is definite and permanent -- I'm reading here from page 1228 of the Burrows Wilcom case. "An idea is definite and permanent when the Inventor has a specific settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue." And we submit that a polypeptide sequence, it's hard to get more settled and permanent and specific than that.

JUDGE TIERNEY: Well, do you want to address what your opponents brought up in the Hintzman vs. Rodderick (ph.) case, a bare hope is insufficient to establish conception?

MR. KREEGER: I'm sorry. I just couldn't hear the question.

JUDGE TIERNEY: Your opponents pointed out, through the Hintzman case, that a bare hope is insufficient to establish conception. And are we at the level of bare hope here, or are you suggesting that there's more?

MR. KREEGER: No, in the Hintzman case, there wasn't a specific sequence, there was a plan, and that's what it was, a hope. This was the sort of research plan type of case. Here we've gotten beyond a hope. I'd submit that the hope was the kind of plan she had when she showed up in Emeryville and began this experimental work. The plan and the specifics comes in the sequence.

JUDGE SCHAFER: What's the history of this, of how this paper, this Exhibit 1106, how was it prepared and modeled?

MR. KREEGER: All right. Well, actually, this will be helpful. We'll turn to Exhibit 1111, which relates, in part, to this. So the Sand (ph.) case says that contemporaneous documents are the best corroborators, so I want to spend my time, my limited time with you today speaking about the contemporaneous documents. Exhibit 1111 is an e-mail from David Pot, who was at Chiron in Emeryville, where he was outlining what Dr. Masignani's (ph.) project was. She was one of the Inventors. She arrived in Emeryville. She ordinarily worked in Sienna. She came to Emeryville because they had the computing facilities to help her for this project. And it really confirms her plan. It says that she's coming to Emeryville in August, she's going to stay a month, which shows that she did her work in the month of August, 1997; she was going to work with sequences that have been released by the Institute for Genomic Research, and her plan was to look for neisseria meningitidis sequences using

bioinformatics techniques to find extracellular molecules that could be used as vaccine candidates, and it goes into the criteria she's going to use, including homology to other known organisms to see if they would be good candidates. And that's exactly what her plan was, that's exactly how she testified to her plan, and it confirms both the date and the existence of the plan.

Then we have Exhibit 1106 itself, and the testimony here is that Dr. Masignani says she generated it on August 13th, 1997.

JUDGE SCHAFER: How was that? Give me some details. How was it generated?

MR. KREEGER: Oh, okay. So this now, we're talking, you know, her testimony. She said she had a series of sequences that had been released by this TIGR, it's referred to, The Institute of Genomic Research, and she began searching them and began to find homologies between those fragments with other organisms, and eventually, she -- and if she could, she tried to stitch them together to create longer contigs or longer sequences that might be more useful, and eventually, she found this one, and others. She had about ten candidates, I think she testified to, that were strong candidates. And this one, once she realized that it could be -- two different sequences could be joined to create the longer sequence, and that that longer sequence had a high degree of homology to this influenza surface protein, she identified it as a very strong candidate for further research, and that's what the printout -- was the basis for the conclusion.

JUDGE SCHAFER: Well, how was the printout made? I'm still -- she was piecing things together, but how do we get to that, the printout from

that? Did she grab certain data and say, oh, here, please put these together for me?

MR. KREEGER: No, she did the work herself. She did it on a computer, and she took the sequences and aligned them and joined them to create the longer contig. She named that longer contig GNMAA-84R. So this is an alignment between GNMAA-84R and the HSF sequence, which was in a publicly available database. Although it was posted on Chiron's servers, it was a public database similar to, you know, the kind of depositories people do when they run blast searches today. And she basically blasted the GNMAA-84R against all known sequences out there and discovered this homology.

JUDGE SCHAFER: Okay. So she puts the things together and says now go search for this and see what's close?

MR. KREEGER: Yes.

JUDGE SCHAFER: That's what's going on. Okay.

MR. KREEGER: Exactly. So what we have here -- and then we have Dr. Pot's testimony that goes through in detail about the distinctive qualities of this printout and how consistent it was with the way the Chiron system worked that further establishes the authenticity. The date shows that it was made in the relevant time period when she was known to be at Emeryville. And he remembers setting up a special directory for her to work, which is -- you'll see it on the printout, it says Z3/U1/PotD -- that was his name -- /Vega. That's Dr. Masignani's first name. That was the directory he set up for her specifically to record her, the results of her work.

So under the rule of reason, you're supposed to ask does this all hang together, does it make sense? And we submit that it does; that the

independent non-Inventor testimony confirms and is completely consistent with the story that this was the time when she was doing her work, this is a printout that shows that it was made from Chiron in Emeryville, it's consistent with her story, and corroborated. I would also point out the several cases that establish that physical evidence such as this document, 1106 and 1111, are the best forms of corroboration of Inventor testimony.

Finally, I want to address this point about the -- after they left Emeryville, they made a slight change to the sequence. They deleted a particular nucleotide which had the effect of extending the reading frame even longer. So this is one nucleotide change. And our opponents make a big fuss about this in saying that it somehow undermines the definiteness or the completeness of the conception, and that, again, completely misunderstands the legal standard. This particular sequence was conceived, and it's within the scope of the count. A later sequence that is even larger was conceived at the time they filed the patent application, and that's also within the scope of the count. The fact that they made that change doesn't say that there was constant flux. Just the opposite; it's a very minor change that actually had the effect of making an even larger protein that was within the scope of the count. But both of them are completely conceived at the relevant time period.

And I guess I'd like to reserve the remainder of my time to respond to Ruelle, unless there are further questions.

JUDGE LANE: Thank you.

MR. KREEGER: Thanks.

JUDGE LANE: Mr. Olstein?

MR. OLSTEIN: Just a moment of time to respond to our priority case. One, on the diligence, the arithmetic that was presented by Scarlato is a little wrong because he left out the weekends. So it's really 6 out of 23, not 6 out of 31. So that's number one. And we've already set out our position that the cases he sited were standards for the Inventor, not standards for someone doing work on behalf of the Inventor, of accounting in detail for every day. The two cases that I cited in the beginning, and then in the Brief, shows that when someone else is doing the work and they have other duties and there are delays in doing it, those are considered to be excused for the purposes --

JUDGE LANE: Is there a different standard when they're both working for the same person? Like Mr. Kreeger was saying, it's not like the situation where you send something out for testing at an outside laboratory that --

MR. OLSTEIN: In both -- I'm sorry, Your Honor.

JUDGE LANE: Go ahead.

MR. OLSTEIN: In both of those cases it was internal. In one, it was graduate students working in the laboratory of the Inventor who were part-time students. In the other one, it was a large pharmaceutical company in which the laboratory, from doing all the testing of the compounds, was backed up. They had a shortage of test animals in that case rather than a shortage of people, and they weren't able to get to the testing.

The other thing I want to address is, again, just briefly, to remind the Court that non-working parts in Dr. Pullen's notebook were clones, single cells of the entire collection. And the testimony that was given by the expert, when asked in cross-examination, the questions were directed to

clones, not to the entire population of clones. And when they said, yes, at times we find clones or individual cells that are not expressing, that is not an admission or testimony that when you have a collection of cells, that you wouldn't have expected it to express once you had experience with the vector and the expression system.

JUDGE SCHAFER: So that first set where it was held at 30 degrees, the first set, the first test or the first experiment and it was at 30 degrees, that was a collection, that wasn't separate clones?

MR. OLSTEIN: That's correct.

JUDGE SCHAFER: And then when you repeated it and did the confirmatory test in 2009, that again was done on the collection?

MR. OLSTEIN: It was done on a clone from the collection. But you've got to remember, if a part of the whole is expressing, then the whole is expressing.

JUDGE SCHAFER: Okay. So what you're saying is that when cloned, that -- from what he was saying, there was one clone that did express?

MR. OLSTEIN: And five that didn't.

JUDGE SCHAFER: And five that didn't. And what you're saying is, that particular clone was in the earlier test?

MR. OLSTEIN: The six -- you've got to remember that there was --

JUDGE SCHAFER: Yeah, there were six, and you had a collection. And I take it's the collection --

MR. OLSTEIN: There's hundreds of thousands of cells in the collection.

JUDGE SCHAFER: Right.

MR. OLSTEIN: You take six cells out of the collection, out of the hundreds of thousands, and that's called a single cell, and then you grow up that single cell into a multiplicity of the same cell.

JUDGE SCHAFER: Okay, my question goes to how do you know that particular cell that you used later was also the same identical type cell that was in the collection earlier?

MR. OLSTEIN: Because it is the same -- it was saved. In other words, if you read our evidence, it was in a refrigerator, there was a whole line of testimony that it's the same one, had Pullen's name, dates, and all the rest of that.

JUDGE SCHAFER: I see. Okay. And then certain ones were selected out of that, and at least one of them --

MR. OLSTEIN: Was saved.

JUDGE SCHAFER: -- expressed?

MR. OLSTEIN: Yeah. But the fact that those five individual cells didn't express doesn't have anything to do -- it's a red herring.

JUDGE SCHAFER: Yeah, I understand that. I'm just trying to make sure that I understand.

MR. OLSTEIN: No, what was saved was the working clone. That was saved.

JUDGE SCHAFER: What was saved was the collection, and the --

MR. OLSTEIN: No, not the collection, the working -- the clone that was tested that was part of the collection was saved, not all of the cells.

JUDGE SCHAFER: Okay. So it was removed from the collection early on and saved?

MR. OLSTEIN: Correct. And tested in February.

JUDGE SCHAFER: Okay.

MR. OLSTEIN: And then it was saved.

JUDGE SCHAFER: And then that same one was tested again at 30 degrees, later?

MR. OLSTEIN: In 2009.

JUDGE SCHAFER: Yeah.

MR. OLSTEIN: So it's the same -- it came out of the collection, all right? It was multiple cells, because you take a single cell and you grow it up into multiple cells. But that was a sample that was saved from the original, and there's a -- it hasn't been challenged by Scarlato, the history and the evidence. You know, we traced it through the label. There was testimony of the person that put it in, that got it back out. So that is not challenged by Scarlato.

JUDGE LANE: Is the testimony such that we could conclude that everything was done exactly the same way in April of 2009?

MR. OLSTEIN: Yes. And that, again, wasn't challenged by Scarlato. If he thought that it wasn't done in the same way, he had an opportunity to comment on it and to --

JUDGE SCHAFER: No, what Judge Lane's getting at is when you move for benefit, you have the burden separate from a challenge or not. Even if they had decided to not show up at all, you still have the burden to prove your case.

MR. OLSTEIN: And our Declaration --

JUDGE SCHAFER: I mean, so that's what the question goes to: Were the things identically done so we feel confident that they reflect what existed earlier?

MR. OLSTEIN: And the answer to that question is the expression was performed in the same way, under the same conditions, and that's what the Declarations say. You can read the conditions and compare it one to the other. They were the same. So I agree it's our burden of proof, I'm just making the point that it wasn't challenged. And I would assume if there were holes and there were differences, that Scarlato would have raised that immediately.

So now, if I may go on to Scarlato's case, in Exhibit 1106, which I hope Your Honors still have, I think there's a fundamental misunderstanding of what 1106 is. And I would like to start off by saying what 1106 demonstrates is what I would call computer conception. The computer conceived something. What do I mean? And it doesn't show that the Inventors had and understood what was done.

So what happens? If you look at Exhibit 1106, they start out with a polynucleotide. We don't know where that came from because -- except from the Inventor's testimony, uncorroborated. That polypeptide is taken by -- polynucleotide is then taken by the computer and translated into polypeptide. And what happens there, there's six frames so there's six possible polypeptides. Then what the computer does is then ran a search automatically of the polypeptides that were created from that polynucleotide, again unidentified, and came up with one of the polypeptides that had a high homology to the HSF protein that you see in 1106. Now, the dates and the times that are shown in here, as Dr. Pot testified in his Declaration, and as we pointed to, merely shows when the computer made the calculation. So if you look at the second line, on Wednesday, August 13th, 9:56 was when the computer did the translation, as I said, of the polynucleotide into polypeptide

sequence. At 10:09 on August 13th, the computer now did a homology search, completed it, and came up, apparently with the sequence comparison of the GNMAA to the HSF protein.

JUDGE LANE: But the computer was doing what it was told to do.

MR. OLSTEIN: That is correct.

JUDGE LANE: Right. I mean, someone had to --

MR. OLSTEIN: Told it to make a query on the polynucleotide. Someone pressed a button. But I'll get back to what it was, but my point here at this point is, all this indicates is that deep on a hard drive in the computer, this information is recorded. But it doesn't show and doesn't tell anyone when the Inventor saw it. So if I do a computer calculation that gets put into the hard drive, it doesn't mean that this was printed out, that the Inventor ever looked at it, ever appreciated what the sequence was, ever saw the sequence, or ever saw the comparison. All this piece of paper does by itself is show that somewhere in the computer this information was stored and the time when it was stored. There's no conflict in that testimony. If you read Dr. Pot's Declaration, that's clearly what he says. Now, how --

JUDGE LANE: Well, is it reasonable to think that the Inventor went down for this specific purpose, to run this type of test, and then would not have looked at the data generated?

MR. OLSTEIN: Well, now you have to understand what the overall testimony was. TIGR had a database. And I'm not going to go in right now, because I don't have the time, is there faults in that database and the sequence accuracy, and all the rest. That's all in our Brief. But there are 2,000 fragments in there. And what Dr. Masignani was doing was typing in computer instructions, take these 2,000 sequences, rearrange them, do this,

do that, and the computer's recording each time it does something, all right, and maybe do sequence comparisons. So I don't know how many comparisons were done. She said in her Declaration they were using the entire TIGR database of 2,000 fragments. So, yes, looking at this individually stored in the file, this is a single piece of paper, but it could have been among thousands of recorded things. Because they were doing what I call shotgun searching of shotgun sequences. By shotgun sequences, randomly sequenced. They were doing random searches. And it's their burden to show when the Inventor first had an appreciation of the sequence, knew it and understood it.

Now, of course, Dr. Masignani and another Inventor said, oh, we looked at it sometime in August, but that's not corroborated. Unlike the laboratory notebooks that Scarlato refers to, in that case you have an Inventor putting sequence down in a laboratory notebook, so you know the Inventor knew what was there at that date, et cetera, et cetera. But when something is in a computer file along with who knows how many other sequences and how many other searches that were done, it's their burden to show when the Inventor first had knowledge of that sequence, and there is nothing of record except this printout. This printout is just a hard copy of something stored in a computer file.

JUDGE SCHAFER: Do you have any doubt that this data existed on the date August 13th?

MR. OLSTEIN: I have no way to -- I do not doubt because I have no way to challenge --

JUDGE SCHAFER: Whether or not --

MR. OLSTEIN: Unless I went and grabbed the hard drive and found that it wasn't there, I have no way.

JUDGE SCHAFER: Right. Your position is we don't know when the Inventor knew this.

MR. OLSTEIN: That's correct.

JUDGE SCHAFER: But you don't have any doubt that on August 13th of '97, that this particular bit of data existed in the form that's shown here?

MR. OLSTEIN: In the computer? I have no way to challenge that. I have no reason to challenge that it existed on a hard drive, or whatever it's called. I'm not a computer expert, but somewhere in some file, it existed.

Now, so, what we're depending on is uncorroborated testimony of the Inventor that she saw this prior to our conception date. We don't know that because there's nothing on this that has any date of when this was printed out, that verifies when it was first available to the knowledge of the Inventor, this sequence. So that's what I meant by computer conception. The computer saw it. The computer, maybe, appreciated it. But I don't know from this record when the Inventors first appreciated it, and all we have is their uncorroborated testimony that they saw it. And again, as I said, it's not a single thing that was being done. There were thousands of sequences that were being looked at by pushing --

JUDGE LANE: What's your evidence that thousands of sequences were being looked at?

MR. OLSTEIN: Because they said that they downloaded the 2,000-and-some-odd sequences from the TIGR database, which is the meningitidis database, into their database to then assemble and do comparisons. And the

general testimony, okay -- and I'll go into the specific corroboration by Pot and the other people -- was that this was a gigantic project; they were going to search through the entire database, starting to look for sequences in that database that had homology to known sequences, and then out of those known sequence -- then look and see from those known sequences whether those sequences met a certain category which were either virulent sequences, a certain type of leader or peptide sequences, and then out of that, go out and select certain sequences for further looking, for further investigation. So by their own testimony, there were thousands and thousands of sequences sitting in this computer, they were all being compared and being searched into the database for homology, so it's their burden to show when the Inventor first appreciated it.

JUDGE SCHAFER: Is there any doubt in your mind or any reason why we shouldn't believe that Dr. Masignani -- and I'm talking about Exhibit 1106.

MR. OLSTEIN: Yes.

JUDGE SCHAFER: Put in the sequence into the computer that's here? I guess it's the GNMAA-8, it looks like.

MR. OLSTEIN: Well, she said that's what she did, but then again, if you read our Brief and you read her deposition testimony, which we did, her memory of what she did is so vague. She testified there were four or five different things that were done. So for all I know, she didn't enter the GNMAA-84R; that that, again, was created by the computer based on the TIGR database, searching the TIGR database in order to put the contigs. It's not a question that she necessarily put the two fragments together to make a longer fragment and then independently went and did the search. That's

what she said she did, but then she said she did a lot of other things. But again, all of that is uncorroborated.

JUDGE SCHAFER: So is your position this was -- they just had a computer program that looked for stuff and threw it all together, and then came up with just thousands of possible reports?

MR. OLSTEIN: And then those reports would have been examined.

JUDGE SCHAFER: How's that different from what everybody else in biotech does?

MR. OLSTEIN: Well --

JUDGE SCHAFER: Isn't that what you all do? I mean, when you get down to it, you have these sequences out there and you're looking for matches and --

MR. OLSTEIN: Well, that is correct. But the difference is --

JUDGE SCHAFER: So nobody's inventing?

MR. OLSTEIN: No, that's not what -- no.

JUDGE SCHAFER: I mean, it seems to me that that's how the invention seems to work in the biotech area.

MR. OLSTEIN: But, you see, our point is not that. Our point is, is what happened in Ruelle's case, he did do that search. But then there's a documented time and date when he printed it out. There's a documented time -- when I say time, date, not the time -- when he handed that sequence off to someone in their laboratory notebook, so you know exactly -- what we have here, I said, is a document which, by their own testimony, just says when the computer file was created. Everything else is Inventor testimony.

Now, I know they talk about the Corroboration Declarations, but the Corroboration Declaration says we know that she was going into the TIGR

database with these couple of thousands fragments, or shotgun sequences as they're called, and she was going to try to piece them together and try to look for homology searches and do that, but that's general. It doesn't show this was seen by the Inventor. It doesn't show -- I mean, if you just look at this document by itself, which is the corroboration document, all that shows it was stored in a file -- that's a so-called Vega file in Masignani's file -- it doesn't show who actually entered the sequence or where it came from, assuming that that entire sequence was entered. I know she said she did, but that's uncorroborated. So what we really have here is a document that's so indefinite that it doesn't establish a date. It was their burden. The only date they've asserted is August 13th. That's the conception date they've asserted. They haven't attempted to prove any other date. And all this shows, at best, is there was a file in the computer that had this sequence.

JUDGE LANE: Now, Mr. Olstein, you want to wrap up?

MR. OLSTEIN: Yeah. Just want to touch briefly on -- the other parts, I'll rely on the Brief, because Dr. Dyer explains why. And I want to point out that a question was asked whether the count required it to be a meningitidis sequence. If you will look at Scarlato Fact 76, they clearly and unequivocally say in their fact that the immunogenic fragment of the count is a native protein fragment, and they define it as a native protein as a Men-B (ph.)protein. So, on this record --

JUDGE LANE: But it is, right? I mean, we know that to be the case now?

MR. OLSTEIN: Yes, but what they're -- yes, we do. But saying that it -- the whole idea of this thing, it can't be something that's random. In order to have a permanent idea of something -- and we explained why, from

the database, you'd have no reason to believe that this is a real sequence, and that's the -- I'm going to rely on the Brief because I'm out of time. The only last thing is the state of flux. What Scarlato alleges is a small change, it's not a small change. And what has to be the definite permanent in the Inventor's mind -- at some point they must have seen this sequence, but they weren't yet satisfied with that sequence because, as I said, the computer generated this, now we have the hand of man, right? What does the hand of man do? It looks at this thing and says, I'm not so sure this sequence is correct. Yes, they only found one error, as they said, which is a major error; significantly changed the protein. It's all in our Brief. But they could have found 20 errors. And until they ran that analysis to look at it and find out whether this was a good sequence or a bad sequence, all they had was a computer-generated sequence, no intervention by the hand of man.

It's only when it came out and was evaluated -- because as Judge Schafer said, what is the Inventor, you know, the human part of this? Well, it's looking at the sequence, evaluating the sequence, deciding whether it's correct or not, what its use is, and what it's purpose is. The computer didn't do that. They did it at some time. I don't know when they saw it. And they clearly knew they had to look at it and evaluate it, and when they did, they found an error. It's a frame shift. It's deleting something; changed numerous amino acids at the front part. So the invention wasn't complete until they looked at it, evaluated it, and made whatever changes they needed to make.

JUDGE LANE: All right. Thank you.

MR. OLSTEIN: No further questions, I will sit.

JUDGE LANE: Thank you. Mr. Kreeger?

MR. KREEGER: Let me just take that last point first. On the definiteness, the Burrows Wilcom case has this comment that if an idea is in constant flux, conception is not complete. But the very next sentence of the opinion says "A conception is not complete if a subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the Inventor's idea, that it is not yet a definite and permanent reflection of the complete invention." And what we have here is a specific idea. The fact that they improved on it and created a longer sequence doesn't undermine the specificity of it as it existed in August.

Now, on the corroboration point on this Exhibit, the rule of reason says you don't throw out the Inventor's testimony entirely, what you do is you ask does the other evidence coming from someone other than the Inventor corroborate their story, does it makes sense. In this case, we have Dr. Masignani say that she generated the GNMAA-84R sequence. Does that make sense? Well, Dr. Pot says that's exactly what she was there to do in a contemporaneous e-mail and his testimony. She took that sequence, she ran this alignment. There's no question that the alignment was run in August. She says she printed it out then, in Emeryville. She looked it over with Dr. Rappuolli when he visited Emeryville in August. That's her testimony. Does the document, you know, on its face, unequivocally establish the date she printed it out? No. Is it consistent with her testimony of that's when she printed it out? Absolutely. It has her handwriting on the top of the printout, which says, in Italian -- we had a translation, I think it's in the record -- "Not in NG," not in gonorrhea.

So this was a sequence that she had discovered, not only that it was present in meningitidis, but it wasn't present in another organism, gonorrhea.

She evaluated the sequence at the time, that's her testimony, and I think the overall evidence, taken as a whole, corroborates that testimony. The rule of reason doesn't require that every specific act be corroborated in the sense that there's a document or an over-the-shoulder observer that's established. You have to ask, on the whole, is this a fraud or is it genuine? And we submit that the evidence shows this is not a fraud.

On the point of thousands of alignments, there's no testimony to that effect. The testimony is that she did many different searches, but when -- she found a small set that she was convinced were strong candidates, and this was one of them. She didn't remember the exact -- I think -- I'm going to from memory here. It's approximately ten candidates that she brought back from Emeryville to Italy as the ones they wanted to pursue, and this was one of them. Does that testimony --

JUDGE LANE: So would she have generated a computer file, or whatever this is, like this for thousands of different sequences?

MR. KREEGER: There's no testimony to that effect. I don't think she was asked, and I don't recall any testimony as to how many computer files like this existed at the time. What she said was she printed out the ones that she was interested in, and it was a relatively small set, and this was among them. That was her testimony, and I think the document is consistent with that.

JUDGE SCHAFER: So she would have been looking for a lot of things simultaneously?

MR. KREEGER: Sure.

JUDGE SCHAFER: Which, I think, is what you all do.

MR. KREEGER: Absolutely. She had a series of criteria, and they're spelled out in her Declaration and the other corroborators' Declarations of how she was going to evaluate these sequences. And one of the key criteria was does it align with a surface-expressed protein that's immunogenic in a related organism? And that's why this was such a valuable hit, because it did.

Lastly, I just want to spend a minute on the Ruelle motion. The claim about these clones, I just want to make sure the record is clear here. There were multiple clones that --

MR. OLSTEIN: Your Honor, I think now he's doing a rebuttal of my rebuttal.

JUDGE LANE: I'm sorry.

MR. OLSTEIN: I apologize.

JUDGE LANE: Yeah, let me -- I didn't follow how -- you jumped up before I was quite following your point. So go ahead, Mr. Kreeger, let --

MR. KREEGER: If the Board will hear me, I'd like to just address briefly the Ruelle motion for my last statement.

JUDGE LANE: Okay. Okay.

Do you think that's okay? All right. Just --

MR. KREEGER: I just want to make sure the record is clear about this clone point, okay?

JUDGE LANE: Go ahead. Go ahead.

MR. KREEGER: There were a series of cells, E. coli cells, and as I pointed out in Exhibit 2038, they were working with three different antigens, three different vectors. Those vectors were introduced into E. coli cells, and then they took multiple clones out. The claim was that they are certain that

it will always express. Maybe a particular clone won't, but they are certain that it will express somehow, and that is just not consistent with the record. Because when it came to the Orph 1-5 antigen, they did not express at all, in any of the clones. And there's a contemporaneous document --

Is that 2069?

MR. LITTLEFIELD: 2069.

MR. KREEGER: 2069. I don't have it here, but there was a document contemporaneous from the time that concluded they did not achieve expression of the Orph 1-5 antigen. And they knew that because they actually did testing. So the claim now that, oh, we knew we were going to express the HSF protein, that is classic hindsight, nunc pro tunc thinking because they couldn't know until they did the tests. And that's what the Orph 1-5 data shows. And with that, I'll submit.

JUDGE LANE: Thank you. Did you want to say something quick in rebuttal to that, Mr. Olstein?

MR. OLSTEIN: I'll say just two things in rebuttal. On the Scarlato motion, he talks about the examination, et cetera, et cetera. My question -- and the printout and the handwriting, it's when. I'll say it again --

JUDGE LANE: I guess I was getting at did you want to say anything about what Mr. Kreeger just said about the cells?

MR. OLSTEIN: Yes, I do, because, again, a clone is a clone is a clone. The fact that the four or five clones that were grown out of the literally hundreds of thousands of cells didn't express just means -- it doesn't indicate that there wasn't expression from the collection of cells, it's just that at that point, they selected clones that didn't work.

JUDGE LANE: All right. Thank you.

(Whereupon, the proceedings, at 2:30 p.m., were concluded.)

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